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Development of Directional Motion Symmetry in the Monocular Visually Evoked Potential of Infant Monkeys

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Motion processing in humans and monkeys exhibit a directional asymmetry during infancy which is not present in adults except following abnormal visual rearing conditions. To characterize the time course for maturation of a symmetric response, we measured the monocular visually evoked potential (MVEP) response to 0.26 c/deg gratings oscillating horizontally at 6 Hz in 13 infant rhesus monkeys between 1 and 52 weeks of age. An asymmetric (F1) and a symmetric (F2) frequency component were extracted from the MVEP using Fourier analysis. At early ages the asymmetric F1 component measured from the two eyes exhibited a 180 deg interocular phase shift, demonstrating that there was a directional bias in opposite directions between the left and right eyes. Although our methods could not determine whether the bias was in the nasal or temporal direction, our results would be consistent with a nasal bias, as has been observed in previous motion studies. Magnitude of the asymmetry was quantified in the form of an asymmetry index, F1/(F1 + F2). Based on developmental changes in the asymmetry index, and phases and amplitudes of F1 and F2, we conclude that the MVEP loses its directional asymmetry at 6 weeks of age. The development of directional motion symmetry observed in monkeys over the first 6 weeks is similar to that observed in humans over the first 5 months. © 1998 Elsevier Science Ltd. All rights reserved.

Motion asymmetry Visually evoked potentials Development Monkey

INTRODUCTION

There is accumulating evidence that both human and monkey infants exhibit directional asymmetry along the horizontal axis for some aspects of monocular motion processing. This has been most widely studied in terms of the monocular optokinetic nystagmus (MOKN) response where infants have been shown to exhibit a stronger response in the nasalward than in the temporalward direction (Atkinson, 1979; Atkinson & Braddick, 1981; Naegele & Held, 1982; Roy, Lachapelle & Lepore, 1989; Lewis, Maurer & Van Schaik, 1990; Lewis, Maurer, Smith & Haslip, 1992; Brown, Wilson, Veira, Goss & Boothe, 1992; Teller, Succop & Mar, 1993). This bias in the neonatal MOKN response has been reported to become symmetrical over the first few postnatal weeks in monkeys, and the first few postnatal months in humans (Atkinson, 1979). However, humans or animals that experience disruptions of normal binocular input at an early age due to conditions such as ptosis, cataracts, or strabismus continue to exhibit asymmetric MOKN even as adults (Van Hof-van Duin, 1976, 1978; Hoffmann, 1979; Cynader & Harris, 1980; Schor & Levi, 1980; Malach, Strong & Van Sluyters, 1981, 1984; Van Hof-van Duin & Mohn, 1983; Sparks, Mays, Gurski & Hickey, 1986; Westall, Woodhouse & Brown, 1989; Lewis, Maurer & Brent, 1989). This implies that the developmental mechanisms responsible for the conversion from an asymmetric to a symmetric response might be dependent on some aspect of normal binocular visual experience.

In addition to these asymmetries in the MOKN response, it has been shown that both normal neonates and adults afflicted with an early onset strabismus exhibit an asymmetry in the monocular visually evoked potential (MVEP) response elicited by stimuli oscillating along the horizontal axis (Norcia, Garcia, Humphrey, Holmes, Hamer & Orel-Bixler, 1991). The extent to which the MOKN and MVEP asymmetries are related to one another is currently unknown. One possibility is that the

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two forms of asymmetry may reflect brain mechanisms that are relatively independent of one another. It is known that the Nucleus of the Optic Tract (NOT) is a critical neural structure involved in generating the OKN response (Hoffmann, 1986, 1989; Kato, Harada, Hasegawa & Ikarashi, 1988; Cohen, Reisine, Yokota & Raphan, 1993; Fuchs & Mustari, 1993), and has been proposed as the neural site responsible for the MOKN asymmetry present in both newborns and in adults who were visually deprived early in development (Van Hof-van Duin, 1976, 1978; Atkinson & Braddick, 1981; Hoffmann, 1982, 1987). On the other hand, the MVEP is derived from a cortical source. Thus, it is possible that MOKN reflects primarily subcortical and the MVEP primarily cortical neural processes. Alternatively, the MOKN and MVEP asymmetries may each reflect specific manifestations of a common neurological asymmetry. Evidence that these two asymmetries are correlated would be suggestive that this latter possibility is deserving of further investigation.

In either case, the MVEP asymmetry may be a useful tool in investigating the development of directionally selective mechanisms, either in the context of normal binocular development or under conditions of visual deprivation. In this paper, we provide data to establish a normal baseline for the developmental time course of the transition to a directionally symmetrical MVEP in the developing rhesus monkey, an animal that has been established as providing a good model of the developing human visual system (Teller & Boothe, 1979; Boothe, Dobson & Teller, 1985; Boothe, 1990, 1993).

METHODS

Subjects

Thirteen rhesus (*Macaca mulatta*) monkeys raised under standard nursery conditions at the Yerkes Regional Primate Research Center were studied. All subjects were judged to be normal at birth by Yerkes veterinary staff, and no eye abnormalities were detected during an ophthalmologic examination carried out by a pediatric ophthalmologist. MVEP recordings were obtained on an opportunistic basis when the monkeys were available for testing at ages ranging from 1 to 52 weeks.

Stimulus

Two different visual display systems were used: a 33-cm video monitor placed at 15 cm from the animal, or a 66-cm video monitor placed at 30 cm from the animal. Each monitor subtended a visual angle of 70 × 56 deg. The stimulus consisted of a vertical 0.26 c/deg luminance modulated cosine grating at 80% contrast with a space-average luminance of 110 cd/m^2. These particular conditions were selected on the basis of pilot studies which demonstrated that this stimulus produced a large cortical response in infant monkeys. The grating changed its spatial phase by 90 deg in one direction, then 90 deg back to its original position as governed by a square-wave temporal modulation at 6 Hz. This horizontal displacement of the grating appeared as an oscillating motion when viewed by a normal human observer.

Procedure

Recordings. The monkeys were first sedated with butorphanol tartrate (Torbutrol) at a dose of 0.05 mg/kg and then swaddled in a cloth blanket and held by the experimenter. Pilot studies demonstrated that this sedative has only a small effect on the MVEP response in terms of a decreased amplitude. The sedative was used to calm the monkeys such that they did not resist having their heads positioned by the experimenter in the appropriate direction for eye fixation on the stimulus. When necessary, small toys and other attention-directing cues, such as tapping on the stimulus display, were also used to attract the monkey's attention and fixation to the stimulus. However, these latter methods were rarely needed, as the sedative usually produced an unwavering stare in the direction in which the head was positioned. Nevertheless, the MVEP recordings were stopped whenever fixation wandered away from the display, and were resumed when the animal's gaze returned to the stimulus.

All recordings were carried out under monocular conditions, with monkeys wearing an opaque contact lens on the non-tested eye. As a control procedure, monkeys were also tested with the stimulus blocked from the view of both eyes to ensure that the MVEPs obtained during stimulus viewing were not due to instrumentation artifacts. The signals obtained under this control condition lacked phase coherence (see below for an explanation of phase coherence), and were indistinguishable from background noise levels.

Subdermal needle electrodes (Rochester Electro-Medical, Inc.) were used to record the MVEP. The active electrode was placed over the left hemisphere of the occipital lobe, between 5 and 10 mm from the midline. Pilot studies revealed that during these unipolar recordings, the left and right hemispheres yield essentially the same results (see also Norcia *et al.*, 1991). The reference

FIGURE 1 *(Opposite).* Development of the asymmetric component F1 (a) and the symmetric component F2 (b), respectively, for a single monkey. The polar plots show amplitude, monocular phase and interocular phase shift information for each trial of a given session at the postnatal week shown next to it. Angle from zero in each plot is the single-trial phase relative to the stimulus onset at 0 deg phase. The solid lines for each vector represent the left eye, and the dotted lines the right eye. The length of each vector is the amplitude of the harmonic normalized with respect to the largest recorded amplitude for that harmonic in that particular monkey (week 2 for F1 and week 7 for F2). Circles represent values for the vector-average of each set of single trials: filled for the right eye; open for the left eye. Note that both the normalized amplitudes and the phases decrease progressively with age for F1, and that the 180 deg interocular phase shift (or bowtie configuration) disappears by week 6. On the other hand, no significant interocular phase shift can be seen for F2, although a progressive decrease in the phases of F2 with age can be observed in each eye.

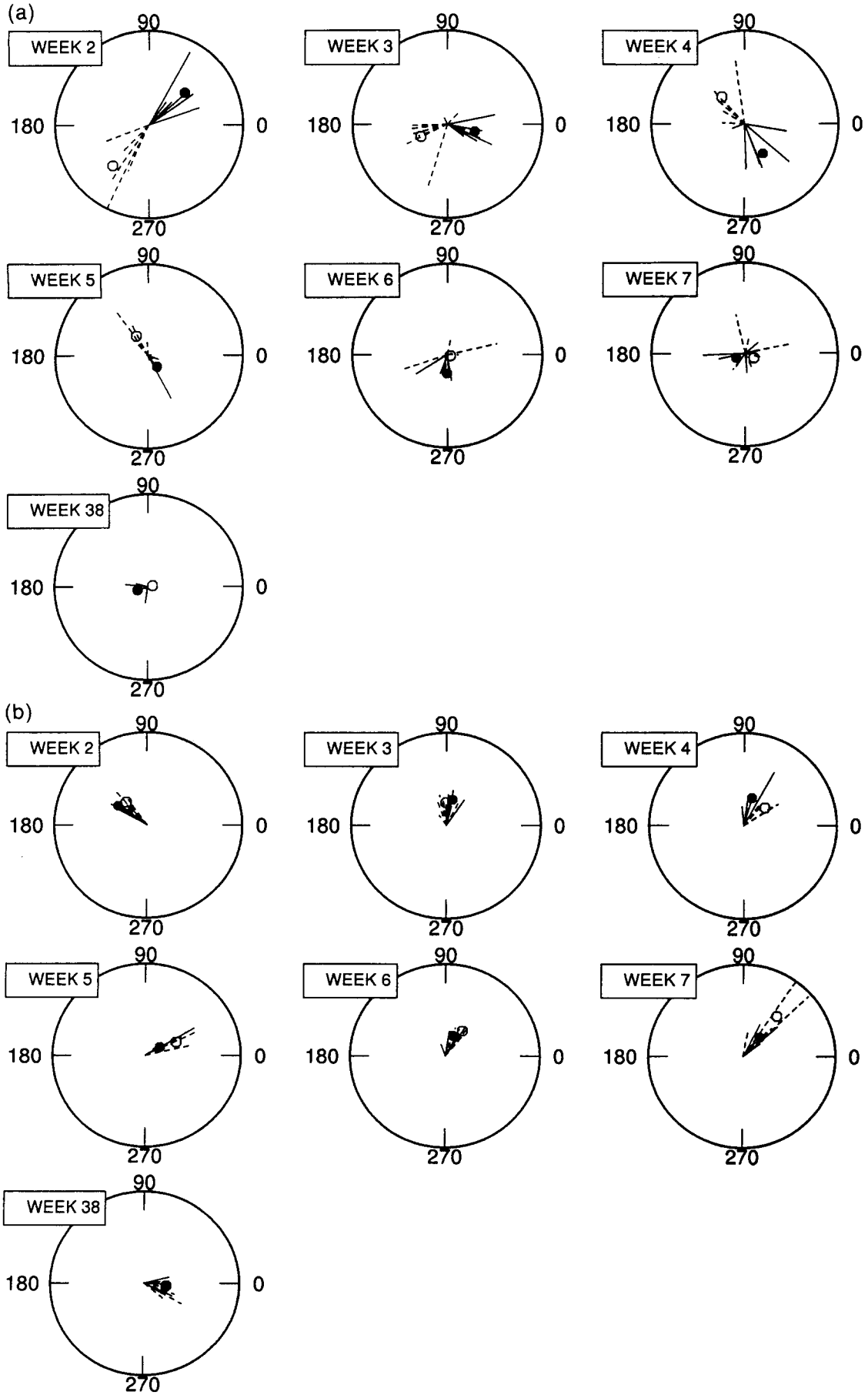

FIGURE 1 *(Caption opposite)*

electrode was placed over the vertex at the midline, and the ground electrode was placed over the right frontal lobe. Each recording session consisted of a series of several trials, each lasting 10 sec. The MVEP was amplified 50,000× with a half-amplitude bandpass filter setting of 1–100 Hz (Grass Instruments, model P-511).

Signal analysis. A Discrete Fourier Transform (DFT) was used to extract the magnitude and phase of the first and second harmonic components of the MVEP. The rationale for the analysis has been discussed previously (Norcia *et al.*, 1991). Briefly, a cortical response during monocular testing is expected for each positional change of the vertical grating. Since there are two such position changes per cycle of stimulus oscillation, one to the left and one to the right, symmetric processing should manifest itself in the MVEP as a second harmonic component. For example, a 6 Hz oscillation should generate a cortical response at 12 Hz, twice the temporal frequency of stimulation. If the MVEP response is larger for one direction than the other, then there should also be a cortical response at 6 Hz, the first harmonic frequency. Individual 10-sec trial responses were vector-averaged across 6–10 trials, by averaging the sine and cosine coefficients of the DFT prior to calculating the response amplitudes. An asymmetry index was used to provide a quantitative measure of the magnitude of the asymmetry:

$$\text{MVEP Asymmetry Index} = F1/(F1 + F2),$$

where F1 is the amplitude of the first harmonic vector-average and F2 is the amplitude of the second harmonic vector-average. This asymmetry index yields a positive value between 0 and 1, with 1 corresponding to complete asymmetry, and 0 perfect symmetry.

Each 10-sec trial also yields a measure of response phase. It is expected that F2, the symmetric component in the MVEP, should have a consistent phase within a session. If a significant amplitude of F1 is present, then the phases of this asymmetric component should also be consistent from trial to trial within a particular session. The Rayleigh statistical test (Mardia, 1972) was used to establish whether a given distribution of phase angles was significantly different from a uniform distribution. Statistical significance ($P < 0.05$) was taken as evidence for phase coherence (see Hamer, Norcia, Orel-Bixler & Hoyt, 1993).

Relative phases in the left and right eyes were also compared in order to determine whether a 180-deg phase shift was present as would be expected if MVEP asymmetry reverses direction across the eyes. Such a reversal would be consistent with, but not direct proof of, a nasalward asymmetry as is present in the MOKN.

Growth curves. In order to characterize the overall shape of the growth curve for the developmental data, we used statistical sample reuse procedures in conjunction with a locally weighted, regression scatter plot, smoothing algorithm (Moses, Gale & Altmann, 1992), implemented with the SPLUS statistical computer software package (Mathsoft, Inc., 1995). We used as a "functional" (cf. Moses *et al.*, 1992) a vector containing the values of the growth curve at each age of interest.

TABLE 1. Age (in weeks) at which F1 is still phase coherent or loses phase coherence

Monkey	Last test coherent	Next test incoherent
Rbq3	4.0	4.4
Rpq3	2.6	3.9
Rsz3	5.3	6.4
Rom4	0.6	6.4
Rvl4	3.0	8.0
Rzh4	5.0	12.1
Rjl4	2.6	—
Rec4	—	15
Rqb4	—	31
Rab4	—	36
Rbo4	—	52
Rku3	—	46
Rro4	—	55

—, monkey not available for testing; decimal point indicates fraction of number of days in the 7-day week.

These procedures are applicable for datasets such as ours that include a mixture of cross-sectional and repeated measures (Moses *et al.*, 1992), and allowed us a means of fitting a growth curve through our data points that was relatively unbiased by our expectations about the shape of the curve, except for the fact that we constrained the curve to vary smoothly rather than being allowed to exhibit discontinuities.

RESULTS

The longitudinal development of the asymmetric and symmetric components of the MVEP response, F1 and F2, are illustrated for a single monkey, Rsz3, in Fig. 1. Results for this monkey were chosen for display because a large amount of data were obtained at regular intervals (once per week) early in development when the asymmetry was expected to be most prominent.

An examination of the F1 polar plots shown in Fig. 1(a) reveals the following: (1) the F1 amplitudes were largest at the youngest age and decreased progressively with age; (2) the phases of F1 were separated by approximately 180 deg across the two eyes through week 5. These "bowtie" configurations are similar to that reported by Norcia *et al.* (1991), and indicate that the direction of the asymmetry was opposite in the eyes at these young ages; and (3) the phases in each eye shifted progressively in a clockwise direction, consistent with a decreasing latency of the response (lag between the stimulus position change and maximum response amplitude), as would be expected as the visual system undergoes myelination.

The F2 response, shown in the polar plots in Fig. 1(b), reveals the following: (1) there were no obvious changes in F2 amplitude with age in this monkey (see below for group results); (2) the phases in the two eyes were similar to one another at any given age; and (3) there was a progressive clockwise shift of phase with age, again consistent with a decreasing latency.

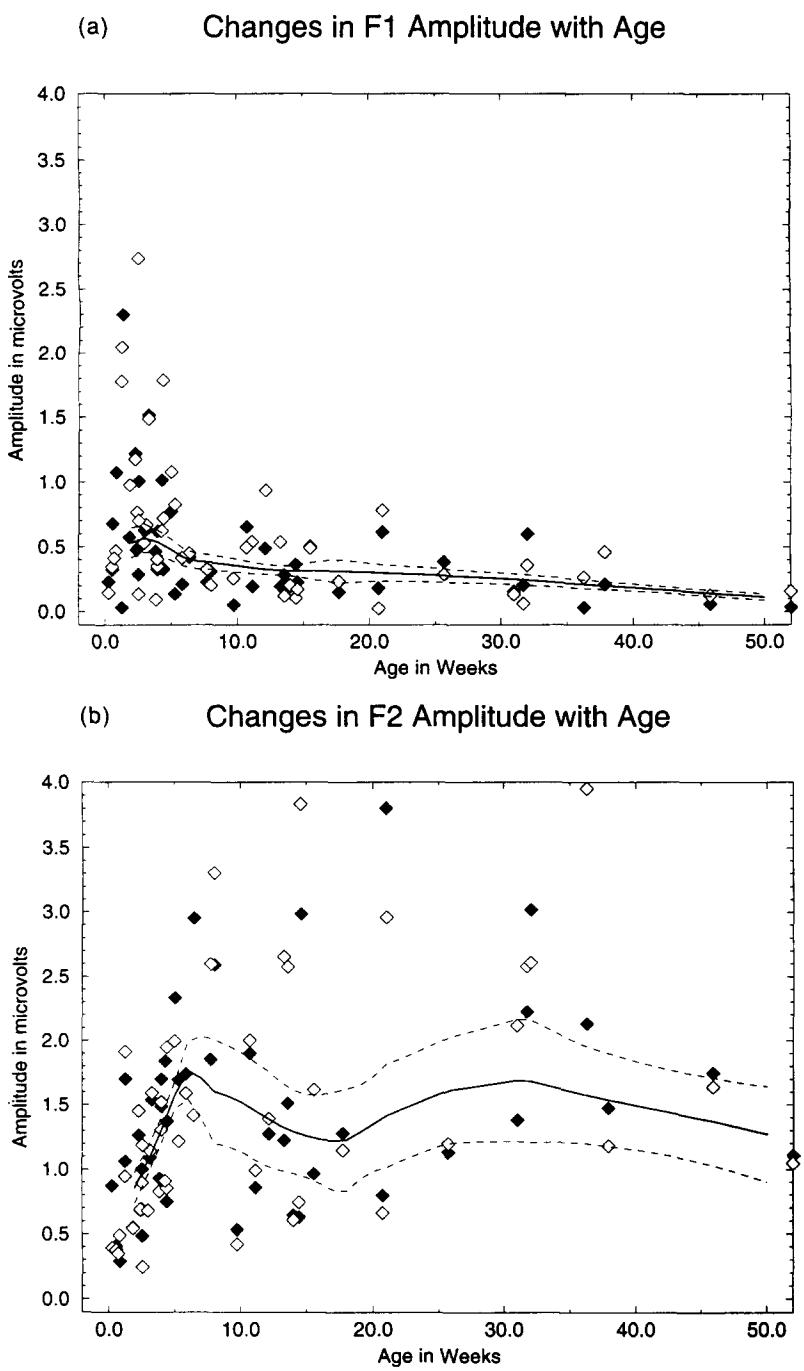

FIGURE 2. The development of the amplitude of the F1 (a) and F2 (b) responses for the group. Each data point represents the amplitude of the harmonic in microvolts plotted for one eye of one monkey and vector-averaged over a single test session (6–10 trials). Open symbols represent left eye and filled symbols right eye data. Monkeys were tested on an opportunistic basis, and as a result these data include a combination of longitudinal and cross-sectional sampling. The smooth lines are the best-fitting growth curves derived from this dataset and the dashed lines designate ±1 SEM.

Phase coherence

We attempted to determine the age at which the F1 component for each individual animal was no longer detectable, based on the age at which F1 first lost its phase coherence using the Rayleigh test. Since phase coherence tests were done separately for each eye, we conservatively chose, for each monkey, to use the eye that retained phase coherence for the longest time. Table 1 shows for each of our 13 subjects the age range within which maturity occurred, given this criterion. The numbers in this table show the oldest test age at which F1 phases remained coherent, along with the first test age at which phases were not coherent. The data shown in Table 1 are somewhat variable, but indicate a range of 4–12 weeks within which phase coherence was lost. The mean age at which phase coherence was lost was 6.9 weeks.

The phase coherence values for F2, as assessed with the Rayleigh test, were highly significant ($P < 0.01$), except in a very few test sessions (less than 1% of the

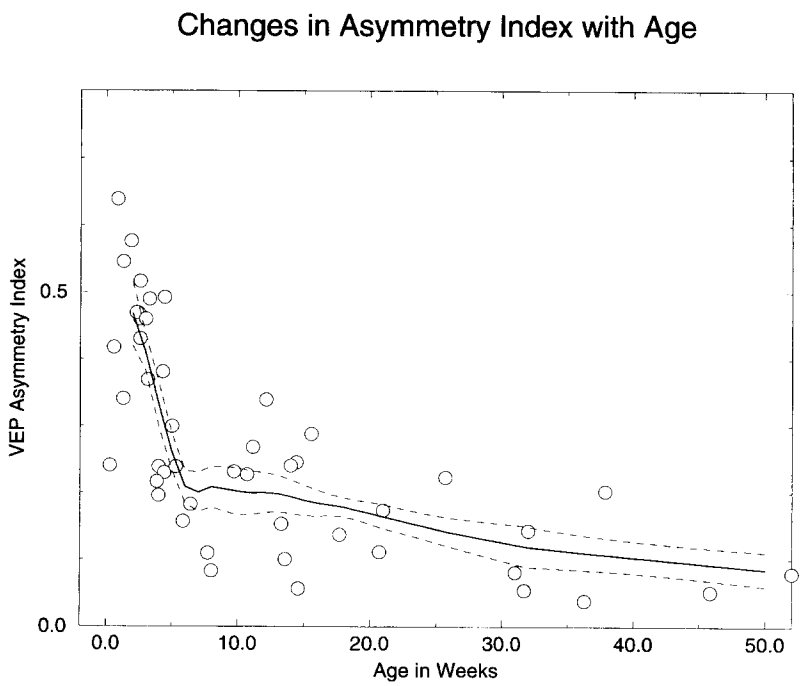

FIGURE 3. Plot of changes in MVEP asymmetry index as a function of age. Data points have been averaged across left and right eye values. The smooth line is the best-fitting growth curve derived from this dataset and the dashed lines designate ±1 SEM.

data). In the latter cases, re-testing the animal in a later session always showed an F2 phase coherence, so the few sessions in which F2 was not significant were eliminated from further analysis of phase relationships.

Amplitude development

Amplitudes of F1 and F2 for each eye of all of our monkeys are plotted as a function of age in Fig. 2(a) and Fig. 2(b), respectively. Left eye data are represented by the open symbols and right eye data with filled symbols. The solid lines are the best-fitting growth curves over the age range of 2–50 weeks and the dashed lines demarcate plus and minus one standard error of the mean (±1 SEM) around the growth curves.

Examination of the data points depicted in Fig. 2(a) reveals that F1 amplitudes exhibit a large amount of variability near birth. Amplitudes vary between 0 and 2.75 μV within the first 3 weeks after birth. Then both the mean amplitude and the variability of the individual data points around the mean decrease. The growth curve fit to this dataset exhibits a rapid decrease from 2 until 6 weeks after birth, followed by a more gradual decline to about 0.1 μV at 50 weeks. This time course is consistent with the longitudinal result shown in Fig. 1(a) for monkey Rsz3.

The F2 amplitude results shown in Fig. 2(b) exhibit a pattern that is roughly reciprocal. Mean values, based on the growth curve, increase between 2 and 6 weeks after birth, and variability of the individual data points also increases over this period. Given the magnitude of the error of the estimate (interval between the dashed lines), the growth curve is consistent with the conclusion that F2 amplitude remains constant between 6 and 50 weeks. These group results are also consistent with the longitudinal data shown for monkey Rsz3 in Fig. 1(b).

Another view of the time course of maturation to symmetry is presented in Fig. 3 in which F1 is normalized to F2 using the asymmetry index. Data for the left and right eyes were averaged from each eye's index and each data point shows the result for a single subject obtained within a single test session. The growth curve, shown by the solid line, reveals that development of the asymmetry index can be characterized by a rapid decline between 2 and 6 weeks of age, followed by a more gradual decline beyond 6 weeks.

In summary, three lines of evidence are consistent with the conclusion that motion asymmetry converts to symmetry at 6 weeks of age: (1) 6 weeks falls within the range within which phase coherence for F1 is lost (cf. Table 1). (2) The period of rapid decline of F1 amplitude ends at 6 weeks [cf. Fig. 2(a)]. (3) Six weeks is also the age when the rapid phase of the decline of the MVEP asymmetry index development ends (cf. Fig. 3). These lines of evidence are elaborated further below in the Discussion.

Developmental changes in phase of the F1 and F2 responses

Figure 4(a) shows an age plot of the F1 phases in each eye from birth to 5 weeks. Absolute values for phase are indeterminate due to the fact that phase is cyclic every 360 deg. We show two cycles on the ordinate to demonstrate the overall changes in phase with age more clearly than would be apparent in a single cycle plot truncated at some arbitrary upper and lower value. Replicated values are indicated with smaller symbols to

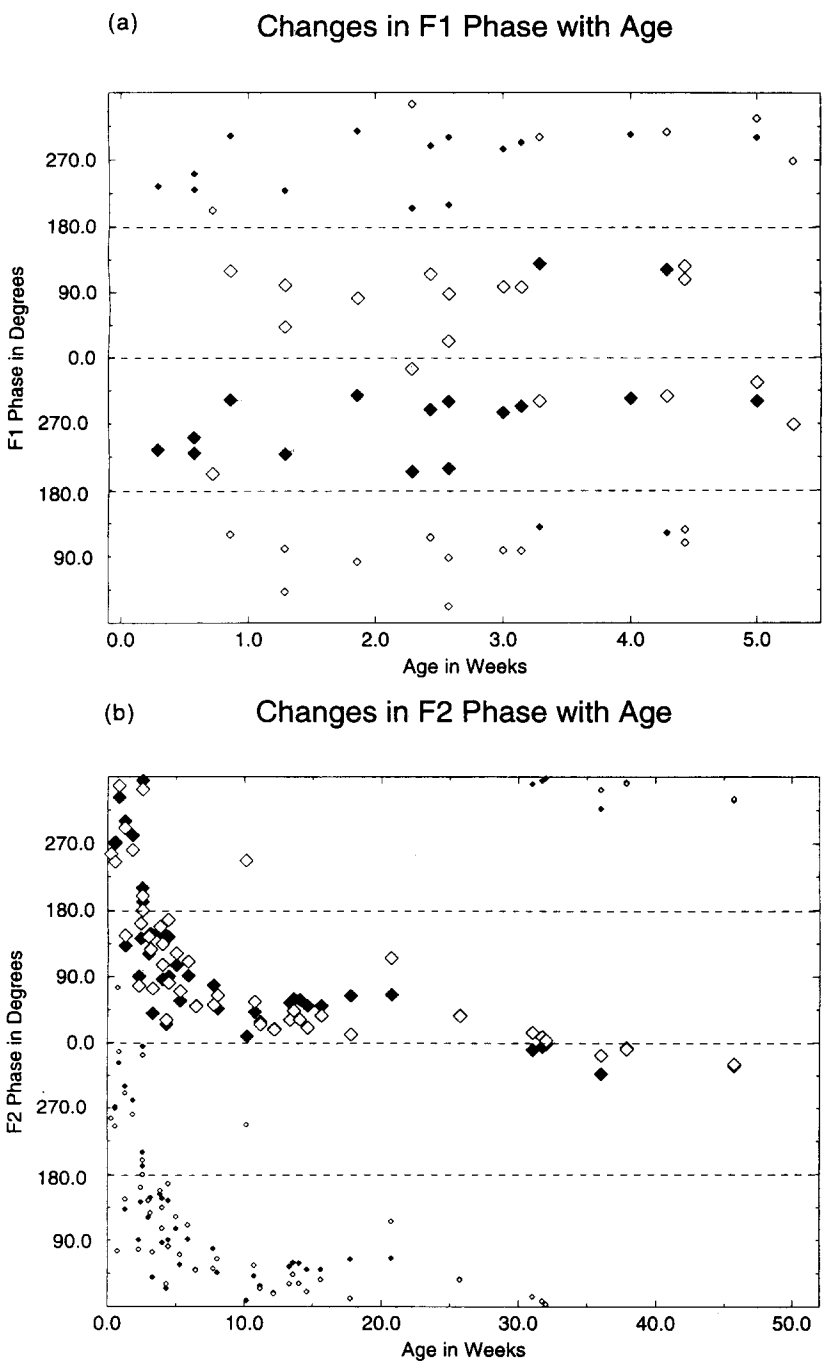

FIGURE 4. (a) is a plot of F1 phase as a function of age. Each point is the vector-averaged phase value for F1 collected during a single test session for a single monkey. Filled symbols represent the right eye and the open symbols the left eye. Since the phase values wrap around every 360 deg, the top and bottom portions of the plot have been replicated to bring points near the (arbitrary) cut lines near each other. Larger symbols are used for one complete cycle of 360 deg, and the smaller symbols are the replicated values. Dashed horizontal lines demarcate ±180 deg from zero. Note that the phases for F1 are clearly separated into left and right eye bands about 180 deg apart during the first 6 postnatal weeks. (b) Shows the development of F2 phase. Left and right eye symbols are the same as in (a). The *y*-axis is also the same as in (a), but the *x*-axis now extends to 52 weeks. Note that the phases for the left and right eyes for F2 at any given age are intermixed, rather than being separated out into separate bands. Also, F2 phases for both eyes are gradually decreasing with age. Large symbols show the data points from one cycle which participate in this developmental trend. Replicated values due to wrap-around are shown by small symbols.

make this wrap-around effect obvious. Examination of the right eye (filled symbols) and left eye (open symbols) reveals that the phases of the two eyes are separated into bands approx. 180 deg apart. For example, it can be noted that 14 out of 20 data points in the arbitrary lower band between 180 and 0 deg are from the right eye, while 11 out of 13 points in the adjoining upper band from 0 to 180 deg are from the left eye. Our overall dataset included 14 pairs of data points where both eyes of a given animal were tested at the same age and the F1

responses were phase coherent in both eyes. Mean interocular phase difference for this group of data was 132 deg (standard deviation = 57 deg). Based on the pattern of results revealed for the longitudinal assessments of one monkey shown in Fig. 1(a), we expected to see a decrease of phase with age. However, examination of the points plotted in Fig. 4(a) does not reveal an obvious trend in terms of a decrease in phase with age within a given eye.

The F2 phases are plotted in Fig. 4(b). The F2 responses remained phase coherent at older ages so we are able to plot values over the entire range of ages tested. If one examines only the results from the first 5 weeks, it is apparent that the phase results for F2 are very different than for F1. The right eye (filled symbols) and left eye (open symbols) for F2 are intermixed rather than separated out into bands as was seen for F1 [cf. Figure 4(a) and (b)]. This demonstrates that the phases are similar across the two eyes at any given age. The mean interocular phase difference for a given subject at a given age was only 22.8 deg.

Figure 4(b) also provides evidence that the F2 phases decrease monotonically as a function of age. However, this conclusion requires an inference about which sets of data points cluster together due to the fact that the data wrap around every 360 deg. We have highlighted the set of data points that we consider to reflect the time course of phase development by using large symbols. Replicated data points are represented by small symbols.

DISCUSSION

The current study has characterized the time course for the development of the MVEP with respect to horizontal motion processing in infant monkeys. We measured the MVEP to gratings having a spatial frequency of 0.26 c/deg and 6 Hz oscillation in monkeys ranging between 1 and 52 weeks of age. The MVEP exhibits both a symmetric (F2) and an asymmetric (F1) component at the youngest ages. With increasing age the asymmetric component decreases while the symmetric component increases. We conclude that the response becomes essentially symmetric at 6 weeks of age. Our conclusion is based on an evaluation of several factors which are detailed in the following sections.

MVEP amplitudes

F1 decreased in amplitude rapidly over the first 6 weeks of age and simultaneously reduced its variability. F2, on the other hand, increased in amplitude over the same age range and became increasingly variable. Hence, the two signals exhibited roughly a reciprocal pattern of development. The decrease in F1 during the rapid phase of development that lasts for the first 6 weeks reflects a decrease in the magnitude of the asymmetry. For reasons that will be discussed below (see subsection: *Phase coherence of F1*) the gradual decrease in magnitude after 6 weeks does not reflect a developmental trend from asymmetry toward symmetry.

The corresponding rapid increase in F2 amplitude over the same age range may reflect in part changes that are not specific to motion processing such as changes in skull thickness or improvements in contrast sensitivity, as has been reported in VEPs in infant monkeys (Skoczenski, Brown, Kiorpes & Movshon, 1995), and humans (Norcia, Tyler & Hamer, 1990b). However, such influences would not be expected to have opposite effects on F1 and F2.

An explanation more closely related to motion processing is that the opposite changes in F1 and F2 amplitudes both reflect an improvement in directional selectivity of single cortical units, which has been reported to be rapid between 1 and 4 weeks of age in monkeys (Hatta, Cheng, Smith & Chino, 1996). A general improvement in directional selectivity for units responding to all directions could account for the increases in F2 amplitude. In addition, if there is an initial bias for some directions over others, then development of responsiveness to the directions that were hitherto physiologically weak could account for the decrease in F1 amplitude.

In order to minimize extraneous influences on the absolute amplitudes, we normalized the F1 and F2 signal amplitudes in each animal by calculating an asymmetry index. This index makes it clear that the *relative strength* of F1 with respect to F2 decreased as a function of age, and, thus, the decrease observed in F1 alone was not simply an artifact due to changes in non-visual factors. The utility of the asymmetry index is also made apparent by the fact that the variability observed in the raw amplitudes of F2 after the age of 6 weeks is reduced considerably when using the asymmetry index, implying that much of the variability in F2 amplitudes beyond 6 weeks [Fig. 2(b)] must have been produced by individual differences in signal amplitudes. The same argument applies to the early data for F1, although the effect is smaller.

Phase coherence of F1

Signals at the F1 frequency can be interpreted as being related to a motion asymmetry only if they can be shown to be phase-coherent. The F1 responses were found to have phase coherence at young ages when their amplitudes were also high.

However, there was a subsequent loss of phase coherence at ages beyond 6 weeks. This loss of coherence is also apparent in the progressing spread of the vectors with age for the F1 response in monkey Rsz3 in Fig. 1(a). At ages after phase coherence is lost, one is only measuring the magnitude of the EEG at the F1 frequency, rather than measuring a signal that is related directly to the stimulus. Any decreases in the asymmetry in the index at these later ages simply reflect decreasing EEG levels, the latter having now replaced the F1 terms in the index.

Taken together, these MVEP results indicate that conversion from asymmetry to symmetry for 0.26 c/deg gratings oscillating at 6 Hz takes place rapidly within the first 6 weeks after birth. The gradual decrease in

magnitude of the asymmetry after 6 weeks reflects changes not associated with the stimulus-related asymmetry. This is also consistent with the data on the single animal presented, Rsz3 (Fig. 1). It should be pointed out that the developmental time course of the MVEP symmetry may depend significantly on the spatial and temporal frequencies used (Norcia, Hamer & Orel-Bixler, 1990a; Brown, Wilson, Boothe & Norcia, 1995). Hence, the development of MVEP asymmetry may have not a single, but several, time courses, and the conclusions of the present study only apply to the specific conditions tested.

180 deg phase shift

Under the hypothesis that the asymmetry was reversed across the eyes, i.e., a nasalward or temporalward asymmetry, the interocular phases would be expected to be 180 deg out of phase. The F1 phase results obtained at early ages appear to be separated out into left and right eye bands that are approximately 180 deg apart. However, in some animals only one eye had phase coherence, and calculating the phase shift for F1 across the eyes is meaningful only when both eyes have valid F1 signals. Therefore, we calculated the mean interocular F1 phase difference for a subset of our data where phase coherence was significant for both eyes, and this analysis was consistent with a 180 deg phase shift.

MVEP phase development

The data from Rsz3 showed decreases in both F1 and F2 phases with age, which is consistent with a decreasing latency of response in the cortex. For the group, the F2 phase decreased sharply over the first 10 weeks or so, confirming that the phenomenon was not idiosyncratic of a single monkey. However, the F1 phase for the group did not show a clear decrease with age. We do not have a good explanation for this unexpected negative finding, but suspect that it simply reflects a lack of sufficient data points to reveal the age trend. We have fewer observations for F1 than for F2, in which both eyes exhibit phase coherence. This is due in part to a lower signal/noise ratio for the F1 signal and the limited ages and monkeys over which the F1 response was measurable. We are currently collecting additional F1 and F2 data from very young infants in order to try to resolve this issue.

MVEP asymmetry comparison between infant monkeys and infant humans

Wattam-Bell (1988, 1991) found evidence for directional selectivity by about 3 months of age in human infants using moving random dot stimuli. Norcia and colleagues have also reported evidence for asymmetries in human infants based on the F1 component of the MVEP (Norcia *et al.*, 1991; Hamer & Norcia, 1994). The present findings of an asymmetry in infant monkeys are consistent with these results from human infants. Furthermore, infants of both species have a 180 deg phase shift between the eyes for F1, while adults have similar phases in the two eyes for F1 (see Norcia *et al.*, 1991 for the human data). The time course of the F1 decline for stimuli at 6 Hz and 1 c/deg is about 5 months for humans (Jampolsky, Norcia & Hamer, 1994; Norcia, 1994) and, from the present results, 6 weeks for monkeys. Thus, the rule of thumb that monkey and human infant ages can be related by "weeks-to-months" (Teller & Boothe, 1979) appears to be roughly applicable to these results. However, there may be some differences in spatial and temporal tuning properties in humans and monkeys which complicate attempts to make an exact comparison (Norcia *et al.*, 1990a; Brown *et al.*, 1995).

Is the MVEP asymmetry an artifact due to eye movements?

The fact that counterphase reversing gratings can elicit asymmetric MOKN in human infants (Teller *et al.*, 1993) leads to a concern that our MVEP results might be secondary to eye movements elicited by our oscillating stimulus. However, there are three lines of evidence that MVEP asymmetries are not secondary to MOKN or other forms of asymmetric eye movements such as latent nystagmus. First, the MVEP recordings were done under sedation and no obvious oscillations or nystagmus of the eyes were observed. Second, results obtained from visually deprived monkeys under anesthetized, paralyzed conditions have also shown a motion MVEP asymmetry (Norcia, 1996; Wilson *et al.*, 1998). Third, Norcia *et al.* (1991) showed that even a simulated nystagmus does not induce significant MVEP response asymmetries in non-sedated humans.

Is the MVEP asymmetry generated in the cortex?

There are a number of lines of evidence that the neural processes responsible for the oscillatory motion MVEP are cortical in origin and that area 17 or V1 is the likely cortical area (but see Braddick, 1996). First, owing to its anatomical location on the surface of the operculum, V1 is likely to be the major contributor to the MVEP recorded from surface electrodes over the occipital lobes in monkeys. Second, the asymmetric response can be detected in local field potentials recorded in striate cortex of visually deprived monkeys under anesthetized, paralyzed conditions (Norcia, 1996; Wilson *et al.*, 1998). Third, directionally specific adaptation in the oscillatory motion MVEP has been observed in humans following prolonged viewing of drifting gratings (Chandna, Norcia & Peterzell, 1993). Also, the adaptation effect transferred interocularly, indicating that it was being generated by neurons that are both binocular and directionally selective, indicating a cortical origin for the asymmetry.

Is the MVEP asymmetry related to the MOKN asymmetry?

The asymmetries seen in the MVEP seem to have, at least superficially, similarities with the asymmetries in the form of a nasal bias that have been previously reported in MOKN. The present findings add to

converging, albeit indirect, evidence that the two measures of asymmetry are related to one another.

The 180 deg phase difference between the F1 components in the two eyes is consistent with a nasal bias, as seen in the infantile MOKN. However, a caveat is that our results are equally consistent with a temporal bias as our methods cannot separate these two directions.

The loss of asymmetry during normal development in both MOKN and MVEP appear to be related to some aspect of development of binocularity. Binocular functions are emerging in infant monkeys during the same general postnatal period as the rapid phase of MVEP maturation. For example, sensitivity to horizontal binocular disparities has an onset at about 3 weeks of age (O'Dell & Boothe, 1997), and binocular alignment of the eyes is attained at about 4 weeks (Boothe & Gong, 1992; Quick, 1992).

Additional evidence that binocularity is involved in maturation of MVEP symmetry comes from developmental motion asymmetries which persist in patients who have experienced early disruptions of binocular interaction (Norcia *et al.*, 1991; Norcia, Hamer, Jampolsky & Orel-Bixler, 1995; Jampolsky, Brown, Boothe, Wilson, Tigges, Norcia *et al.*, 1993, 1994). It is well-known that early disruptions in binocularity are associated with MOKN asymmetries (Van Hof-van Duin, 1976, 1978; Hoffmann, 1979; Cynader & Harris, 1980; Schor & Levi, 1980; Malach *et al.*, 1981, 1984; Van Hof-van Duin & Mohn, 1983; Sparks *et al.*, 1986; Lewis *et al.*, 1989; Westall *et al.*, 1989; Tychsen, Quick & Boothe, 1991). A good correlation has been reported between the asymmetries in MOKN and MVEP measures in human cases of early-onset strabismus (Brosnahan, Norcia, Schor & Taylor, 1996, but see also Kommerell, Ullrich, Gilles & Bach, 1995).

The dependence of MOKN symmetry on binocular processing has been theorized to reside in the nucleus of the optic tract (Hoffmann, 1987). Whether the mechanisms responsible for MOKN symmetry reside exclusively in the subcortex or involve some combination of cortical and subcortical regions remains currently unknown.

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